The Diastereoselectivity of Electrophilic Attack on Trigonal Carbon Adjacent to a Stereogenic Centre

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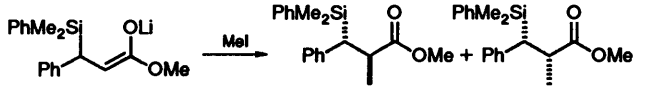
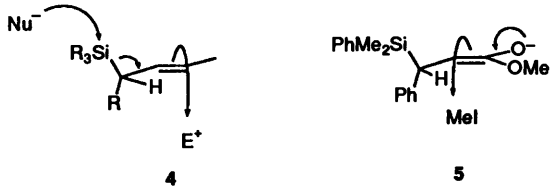
This paper summarises the work described in the nine papers immediately preceding it. The diastereoselectivity of attack on a trigonal carbon adjacent to a stereogenic centre is governed by the general rule expressed most simply by the drawing **34**, except when the medium-sized group on the stereogenic centre is methyl at the same time as the substituent *cis* to the stereogenic centre is a hydrogen atom, when reaction may or may not take place in the sense of the drawing **35**. When the large group on the stereogenic centre is a silyl group, the diastereoselectivity of electrophilic attack is high, as shown by enolate alkylations and aldol reactions, and the reactions of allylsilanes with osmium tetroxide, peracid, the Simmons–Smith reagent and boranes. The protodesilylation of allylsilanes can be used to control the geometry of trisubstituted double bonds, notably those exocyclic to a ring, provided that the medium-sized group on the stereogenic centre is an isopropyl group. Two regiocontrolled syntheses of allylsilanes that are secondary at both ends of the allylic system are reported in the last two papers. The first of the two syntheses gives largely *trans*-allylsilanes, but the second provides good control of double bond geometry with either the *cis*- or the *trans*-configuration. Both syntheses are amenable to the synthesis of homochiral allylsilanes.

Composed at the request of one of the referees, this paper is simply a summary of the nine papers preceding it. It gives an overall view of the most important material and conclusions discovered in the course of this work, and makes a little clearer the shifts in our efforts over the last ten years in response to our discoveries.



1 2 (97:3) 3

Historically, this work began with the observation[1] of what seemed to us at the time to be an unexpectedly high level of stereocontrol in the methylation of the enolate **1**, made by conjugate addition of our silyl-cuprate reagent to methyl cinnamate, which gave the diastereoisomers **2** and **3** in a ratio of 97:3, although to begin with we did not, of course, know which was which. Shortly before we made this observation, both we[2] and Kumada[3] had suggested an explanation for the *anti*-

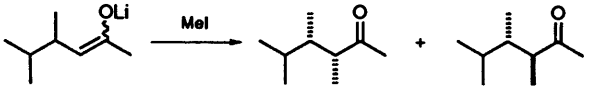


4 5

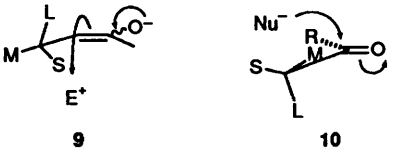
stereospecificity of the S_E2' reaction of allylsilanes summarised in the drawing **4**. We reasoned that this drawing approximated both the lowest energy conformation and the conformation at the time of reaction: the hydrogen atom would be the group more or less eclipsing the double bond, and the electrophile would attack the double bond on the face *anti* to the silyl group for steric, and possibly also for electronic, reasons. Applying the same idea to enolates, we deduced that the stereochemical sense of the methylation would prove to be the same, as illustrated in the drawing **5**, although the regiochemistry was of course different. With one small surprise, we soon showed that methylation had indeed taken place in this sense.[4]

The general subject of the stereochemistry of electrophilic attack on a double bond had been much less well studied at that time than the corresponding nucleophilic attack on a carbonyl group, which had been the subject of Cram's far sighted work establishing that open-chain stereocontrol was rational and predictable.[5] Accordingly we chose to study the stereochemistry of electrophilic attack on a carbon–carbon double bond in more detail, beginning with enolate alkylations in general, aware that Evans had picked this subject out as one for which there was a surprising lack of information.[6]

The first paper in this series[7] sets the scene, discusses the theoretical work, largely of Houk, and describes our work on the methylations of three families of enolates having only carbon substituents on the stereogenic centre. Thus the ketone enolate **6** gave more of the ketone **7** than of its diastereoisomer **8**, in a reaction taking place largely in the sense **9**. This is

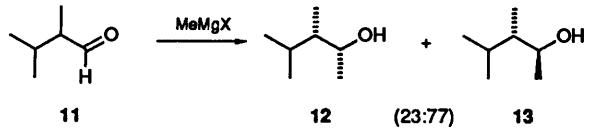


6 7 (75:25) 8



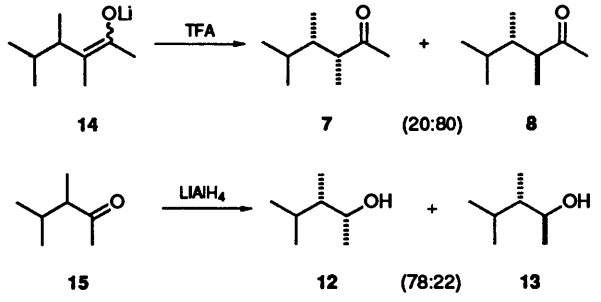
9 10

complementary to the sense of the corresponding nucleophilic attack by methyl nucleophiles on an aldehyde group, which has been explained by Karabatsos, Felkin and Anh using minor variations of the drawing **10** (R = H), in which the medium-sized group M eclipses or partly eclipses the double bond. Thus the direct comparison of our reaction **6**→**7** + **8** with its known



11 12 (23:77) 13

nucleophilic counterpart **11**→**12** + **13**, in which the alcohol **13** is the major product, reveals the complementary nature of the electrophilic (Houk) rule and its Cram (Felkin–Anh) counterpart. We also carried out the corresponding protonation reactions, and the complementary hydride reductions were known. Thus protonating the enolate **14** and reducing the methyl ketone **15** gave the ketone **8** and the alcohol **12**,

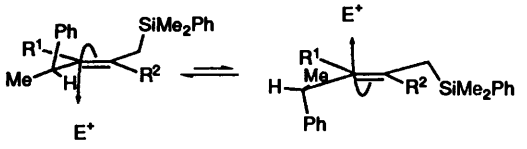


14 7 (20:80) 8

15 12 (78:22) 13

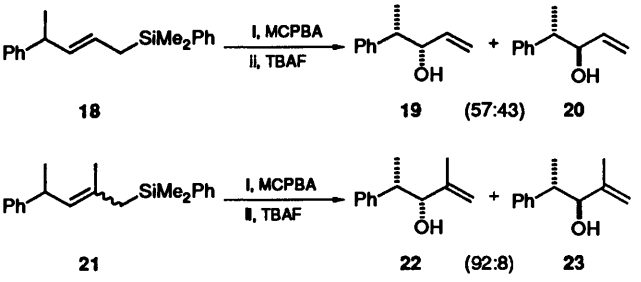
respectively, as the major products, complementary to each other, and, of course, complementary to the earlier results. Our results were ambiguous only when the stereogenic centre carried an isopropyl and a phenyl group, for which it was somewhat uncertain which should count as the large and which the medium-sized group. The electrophilic reactions were straightforwardly in the sense **9**, if the isopropyl group is the large group and phenyl is the medium-sized group. The nucleophilic reactions on the other hand were inconsistent, with Grignard reaction taking place in the sense **10** but, with hydride reduction, which curiously was not in the literature, perversely taking place with the highest selectivity of all (97:3) in the opposite sense to that illustrated as **10**. We concluded that on the whole electrophilic reactions, although later on the scene, would prove to be better behaved and more reliable in their stereochemistry than the corresponding nucleophilic reactions, largely because there was so much less ambiguity in predicting both the lowest energy conformation and the reactive conformation.

In the second paper,[8] we took a representative stereogenic centre, that having a phenyl and a methyl group on it, and changed the nucleophilic double bond from the enolate like **6** to a range of allylsilanes **16**, allowing us to change the electrophile



16 17

significantly. Our conclusions were threefold. The sense of the diastereoselectivity was still covered by the general rule **9** as illustrated in **16**. The nature of the electrophile did have an effect, with chlorosulfonyl isocyanate more selective than peracid epoxidation, which was in turn more selective than protonation or deuteronation. But most significantly, we observed for the first time that the general rule was not reliable in those reactions in which the substituent R^2 on the double bond *cis* to the stereogenic centre was only a hydrogen atom. Thus the allylsilane **18**, which was largely *E*, gave only low selectivity (57:43) in favour of the formation of the alcohol **19**,

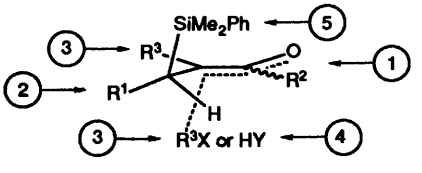


18 19 (57:43) 20

21 22 (92:8) 23

but the allylsilane **21**, although a mixture of *E* and *Z* isomers, gave the alcohol **22** with high (92:8) selectivity. When R^2 is a hydrogen atom, the conformation **17**, with the methyl group on the stereogenic centre on the inside, is not much higher in energy than the usual conformation **16**, and it can be well populated at the time of reaction. Reaction from this conformation, with attack *anti* to the large group is then in the opposite sense to the usual reaction. This problem had not arisen in the earlier work, because all our enolates had had a substituent larger than a hydrogen atom *cis* to the stereogenic centre.

In the third and most substantial paper of the series[9] we returned to our observation of high diastereoselectivity in the methylation of enolates like **1**. We discuss the effect of having a heteroatom on the stereogenic centre, and conclude that, while an electronegative element like oxygen might well lead to some uncertainty in the diastereoselection, an electropositive element like silicon or tin ought to provide high levels of stereocontrol because the conformations are more secure and the steric and electronic effects of these large groups ought to reinforce one another. Clearly the presence of a silyl group had made the diastereoselectivity higher in the reaction of the enolate **1** than we had been seeing with only carbon groups on the stereogenic centre, and so we asked ourselves how reliable and general was this degree of selectivity. We looked at all the variables numbered in the drawing **24**, and found that changes in most of



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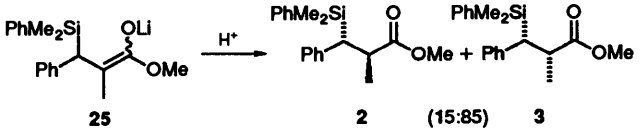
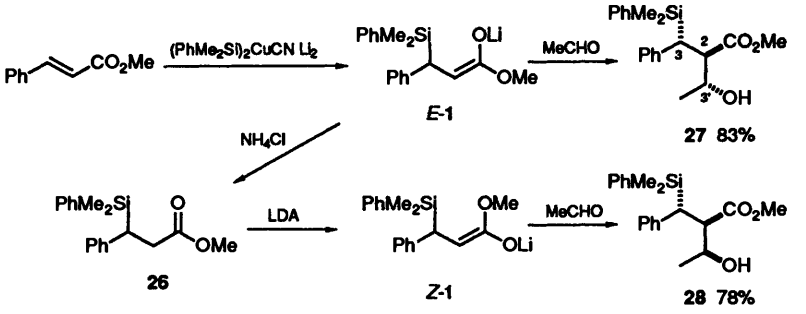
them made little difference. (1) The nature R^2 of the enolate, whether of an ester, ketone or amide, was unimportant, and the geometry, *E* or *Z*, made no difference. The corresponding anion of a nitrile, however, understandably gave much lower selectivity in methylation. (2) The carbon group R^1 on the stereogenic centre made some difference: phenyl was the best, but other large groups, especially *tert*-butyl, reduced the diastereoselectivity in methylation without inverting the sense of that diastereoselectivity. (3) The nature of the alkyl halide R^3X had almost no discernible effect, giving very much the same high level of diastereoselectivity as methylation. (4) Alternatively, having an alkyl group R^3 resident in the molecule, and protonating the enolate, as in the protonation of the enolate **25** giving the esters **2** and **3**, gave the opposite major dia-



25 2 (15:85) 3

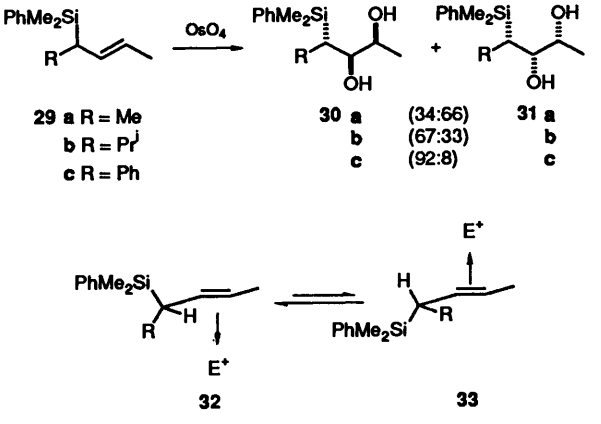


stereoisomer to that obtained in the corresponding alkylation reactions. The ratio of diastereoisomers was affected to a small extent by the nature of the acid used, and the degree of diastereoselectivity was not as reliably or as understandably high as it was for most of the alkylations. (5) Changing the silyl group had a small but not always consistent effect. Thus a *tert*-butyldiphenylsilyl group raised the methylation ratio, analogous to **1**→**2** + **3**, from 97:3 to <99:1, but worsened the protonation ratio, analogous to **25**→**2** + **3**, from 15:85 to 34:66. Finally, keeping R^3 as a methyl group, we used several alkyl halides to set up quaternary centres with high stereoselectivity, but when R^3 was much larger than a methyl group the stereoselectivity was not high.

In analysing the results of all these experiments, we looked for evidence that some of the diastereoselectivity might be controlled by electronic factors as well as by the obvious steric factors stemming from the large size of the silyl group. We argue that the electronic effect of a silyl group should operate in the same direction as the steric, which might explain why a stereogenic centre carrying a silyl group is so effective in controlling the stereochemistry of attack in its neighbourhood, but the evidence in favour of a contribution from electronic factors is weak, depending only upon a qualitative assessment of how relatively hindering a *tert*-butyl and a silyl group might be. There was no evidence that the presence of a silyl group significantly enhanced the kinetic nucleophilicity of enolates like **1** relative to simple ester enolates when we placed them in direct competition for a deficiency of methyl iodide.

In the fourth paper,[10] we moved on to a class of electrophiles left out of the third paper in the series, namely aldehydes and, to a lesser extent, other trigonal electrophiles. These conformed to the general rule that the nature of the electrophile made little difference, all of them giving high levels of control, as in the reaction *E*-**1**→**27**, with only 4% of the product having the alternative stereochemistry between C-2 and C-3. (We use the strict *E* and *Z* nomenclature here, not that often used when discussing aldol chemistry.) These reactions also proved to be highly controlled in the aldol geometry between C-2 and C-3′, the ratio of **27**:**28** being 85:15 from the *E*-enolate, *E*-**1**, and 9:91 from the *Z*-enolate, *Z*-**1**. The sense of the aldol geometry is the opposite to that normally encountered. These reactions have a large group attached to the nucleophilic carbon of the enolate, but a small group on the ester, whereas most aldol reactions of this type are carried out with a small group attached to the nucleophilic carbon of the enolate and a large esterifying group. It was known that this reversal changes the sense of the aldol geometry.[11] Both *E*- and *Z*-enolates are readily available, as we showed in the third paper in the series: the *E*-enolate being produced by the conjugate addition of the silyl-cuprate to an α,β-unsaturated ester, methyl cinnamate in this case, and the *Z*-enolate by regenerating the enolate with LDA (lithium diisopropylamide) from the ester **26**. Thus the 2,3-relationship is always in the same sense, being a consequence of the idea embedded in the drawings **5**, **9** and **24**, and the 2,3′-relationship can be set up in either sense, being a consequence of the chair-like transition structure of the lithium enolate aldol reaction.

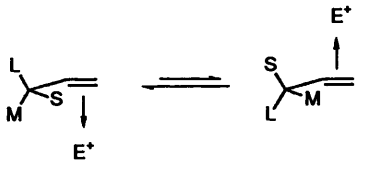
In the fifth paper,[12] we returned to a theme we had worked on earlier, the stereochemistry **4** of allylsilane reactions with electrophiles, this time concentrating on how varying the group on the stereogenic centre and the geometry of the double bond affected the degree of that diastereoselectivity. We looked at the sense of attack on allylsilanes by peracid, by osmium tetroxide and by the Yamamoto version of the Simmons–Smith reaction. In this work we were fleshing out some earlier work by Vedejs and McClure,[13] who had shown that bridging electrophiles like peracid and osmium tetroxide did not always appear to be stereoselective in an *anti*-sense. Thus they found, in their most extreme example, that the *E*-allylsilane **29a** gave the diols **30a** and **31a** in a ratio of 34:66. They argued that an *E*-allylsilane might sometimes react in the lower-energy conformation **32**



(R = Me) and sometimes in the higher-energy conformation **33** (R = Me), depending, amongst other things, upon the size of the electrophile. A large electrophile like osmium tetroxide would attack the conformation **33**, in which it came close only to the hydrogen atom on the stereogenic centre, rather than the conformation **32**, in which it would come close to the R group. In support of this idea they found that the corresponding *Z*-allylsilane reacted cleanly in the conformation **32**, because the alternative in this case, with the methyl group experiencing a bad $A^{1,3}$ interaction, would be much higher in energy and barely populated. We wondered how the change of the group R would affect this picture. Would a larger R group be more effective in biasing the equilibrium in favour of **32**, or would it be more important in hindering the attack of the electrophile in that conformation? We found that the larger R groups isopropyl and phenyl made more of the reaction take place in the stereochemical sense of **32**, and probably therefore in that conformation. Thus, the allylsilanes **29b** and **29c**, with isopropyl and phenyl groups on the stereogenic centre, gave the corresponding diols **30** and **31** in ratios of 67:33 and 92:8, respectively. The corresponding epoxidation reactions and Simmons–Smith reactions were inherently more selective in the

sense **32**, but they also showed an increase in the proportion of reaction taking place in the sense **32** when the R group was changed from methyl to isopropyl or phenyl, although in these reactions, the isopropyl group gave the higher selectivity. All the corresponding *Z*-allylsilanes were highly selective in the sense **32**.

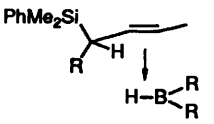
In all this work therefore we came to an important general conclusion: electrophilic reactions in the general sense **35**, with the medium-sized group 'inside', would only be major pathways when the medium-sized group was small, like a methyl group, and the substituent on the double bond *cis* to the stereogenic centre was only a hydrogen atom. In all other situations, either with larger medium-sized groups or with larger groups *cis* to the stereogenic centre or both, electrophilic attack can be expected to take place predominantly in the sense **34**. Houk's calculations



34 **35**

that a conformation close to that illustrated here as **35** was important for electrophilic attack by some electrophiles was carried out using methyl as the medium-sized group. Similarly, Houk's [14] and Curran's [15] experimental observations that nitrile oxide cycloadditions fitted this pattern, also had a methyl group as the medium-sized group. We recommend the simplified and general drawings **34** and **35** as an aid to understanding, while acknowledging that they are not, in detail, adequate for more specific reactions. The lowest energy conformation and that at the time of reaction will not be identical, nor, in all probability, will the small group be exactly eclipsing the double bond. The nature of the electrophile, the nature of the other substituents on the double bond and the relative sizes of the three groups on the stereogenic centre will all affect the dihedral angle at the time of attack, and hence the stereochemical sense and the degree of that stereoselectivity. Until experience enlarges our understanding, it is safe to say that the general rule for electrophilic attack can now be expressed most simply by the drawing **34**, and that the one exception is when the medium-sized group is a methyl group at the same time that the substituent *cis* to the stereogenic centre is a hydrogen atom. With silicon-containing compounds fitting this latter description, our experience suggests that the stereochemistry of attack becomes highly unpredictable, except when there is a close analogy to work from. Some reactions, like the hydroboration of allylsilanes with 9-BBN, show essentially complete selectivity in the sense **32** (R = Me),[16] while others, like Diels–Alder reactions between the corresponding dienes and acetylenedicarboxylate,[17] show essentially complete selectivity in the sense **33** (R = Me). These extreme values bracket the results of Vedejs and McClure with osmium tetroxide, Curran's nitrile oxide cycloaddition, and our own results on the S_E2' reaction of the allylsilane **29** (R = Me and Me_3Si in place of $PhMe_2Si$), which reacts with the adamantyl cation in the senses **32** and **33** in a ratio of 40:60.[18]

In the sixth paper[16] we extended the work of the fifth paper to hydroboration. Our conclusions largely support the general remarks made immediately above: hydroboration takes place predominantly with the regiochemistry and stereochemistry **36**. Thus the *trans*-allylsilane **29c** with borane followed by oxidation gave largely the alcohol **37c**, the proportion increasing, both regiochemically and stereochemically, with more substituted hydroborating agents like 9-BBN (values in parentheses). On the other hand, when the R group was methyl and



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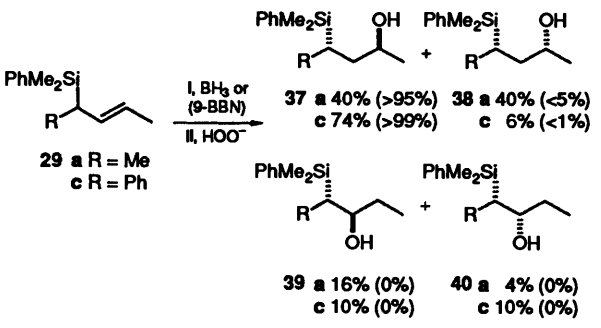
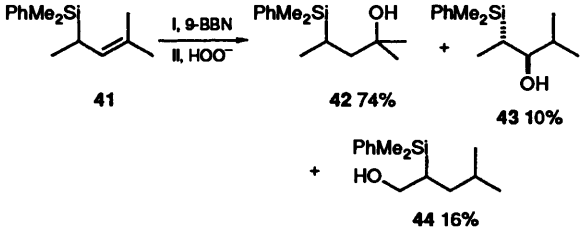
the double bond still *trans*, the allylsilane **29a** was stereochemically very unselective with borane (50:50 for both regioisomers), although surprisingly selective (>95:5) with 9-

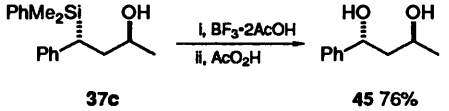


BBN, both regiochemically and stereochemically, as mentioned above. The corresponding *cis*-allylsilanes gave higher levels of stereoselectivity in the same sense **36**, as expected by analogy with our analysis of the results using osmium tetroxide, peracid and the Simmons–Smith reagent described in the fifth paper. Necessarily reaction in the sense **36** on the *cis*-isomer gives the diastereoisomeric product. Thus the *cis*-allylsilane corresponding to **29a** reacting with borane itself gave the 1,3-silylated alcohol **38a** as the major product (79%), with the regioisomer **39a** as the major byproduct (16%). As before, the regio- and stereo-selectivity is essentially complete (95% of **38a**) with 9-BBN, making both diastereoisomers **37** and **38** available by choice of double bond geometry.

The presence of the silyl group contributes substantially to the regioselectivity of these hydroborations. In the most striking example, hydroboration–oxidation of the allylsilane **41**



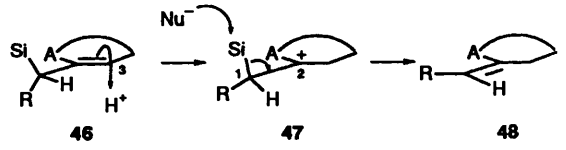
using 9-BBN, gave the alcohol **42** as the major product, even though this places the boron atom at the fully substituted carbon. The isolation of the product **44**, in which substantial migration of the boron must have taken place, shows that this result is not simply kinetically controlled. In this work, we used extensively our capacity to convert the phenyldimethylsilyl group into a hydroxy group with retention of configuration,[19] as in the reaction **37c**→**45**, both to demonstrate that these



reactions are useful syntheses of 1,3-diols, in either stereochemical relationship, and to identify the relative stereochemistry of all the products.

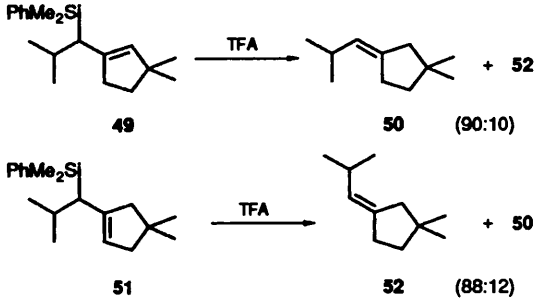
In the seventh paper[20] we applied the knowledge gained in

the earlier papers to control, not a new stereogenic centre, but the geometry of the double bond in the product. If the reactive conformation **46** can be relied upon when the R group is large, the S_E2' reaction of an allylsilane ought to deliver a double

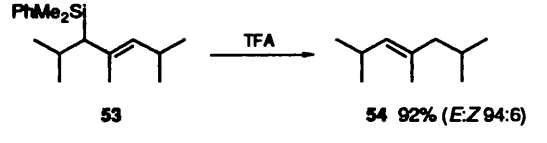


46 **47** **48**

bond with a configuration preserved from that conformation. It is known that protodesilylation of allylsilanes takes place by attack of a proton on C-3 to give an intermediate cation **47**, stabilised by the presence of the silyl group. The silyl group is then lost from this conformation, without rotation about the bond between C-1 and C-2. We studied this reaction with a view to controlling the double bond geometry exocyclic to a ring, knowing from the work described above that the R group would almost certainly have to be as large as a phenyl or isopropyl group, and the A group would have to be reasonably small, if the conformation **46** was to be relied upon. Although the need for A to be small might seem like rather a serious limitation, it is precisely when A is a methylene group that the difference in energy between the alkenes **50** and **52** will be minimal, and when it is therefore most desirable to have a synthetic method that does not depend in any way upon the difference in energy between them. In the event, having an isopropyl group as the medium-sized group R was effective enough to be synthetically useful, the allylsilane **49**, for example, giving largely (90:10) the geometrical isomer **50**, and, in the

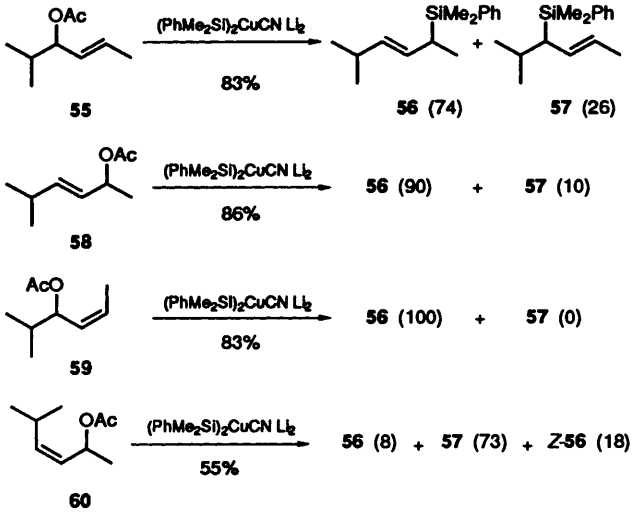


complementary reaction, the allylsilane **51** giving largely (88:12) the isomer **52**. In contrast, a phenyl group for R was surprisingly ineffective. This type of control of the geometry of a trisubstituted double bond is not, of course, restricted to exocyclic double bonds—the open-chain reaction **53**→**54** was also stereochemically well controlled.



The eighth[21] and ninth[22] papers describe our work on the regiocontrolled synthesis of some of the allylsilanes that were used for the work in the fifth, sixth and seventh papers in the series. We had been very early in the history of allylsilane chemistry in showing that the essence of much of it was in the control it gave to the site of attack and the site of the double bond created. We knew therefore how necessary it was to develop regiocontrolled syntheses of unsymmetrical allylsilanes if the full potential of these carbon nucleophiles was to be realised. Our early efforts[23] were very limited in their scope, but established the principle. Later we found good methods for placing the silyl group at the less substituted end of an unsymmetrical allyl system, using either the Wittig reaction[24] or the attack of our silyl-cuprate reagent on tertiary allylic acetates.[25] We also developed one method for placing the silyl group at the more substituted end of an allylic system.[26] But all these methods were unsatisfactory for making allylsilanes that were unsymmetrical and secondary at both ends of the allyl system. Our methods for the synthesis of this class of allylsilane are covered in the eighth and ninth papers.

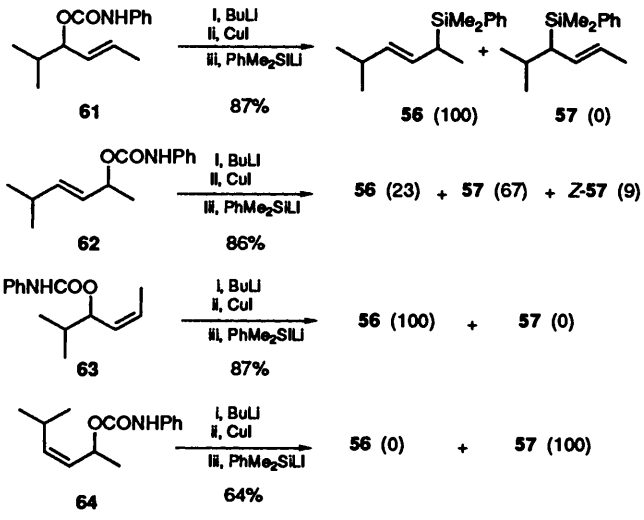
In the eighth paper,[21] we extended our method using the silyl-cuprate reagent and allylic acetates from tertiary to secondary allylic acetates, which had not reacted in our earlier attempts. The trick here was to use a less polar solvent than THF—merely diluting the THF, needed for the preparation of the silyl-cuprate reagent, with ether proved to be adequate in most cases. The major products usually had *trans* double bonds, but the regiocontrol was incomplete if the double bond in the starting material was *trans*, as in the reaction **55**→**56** + **57**.



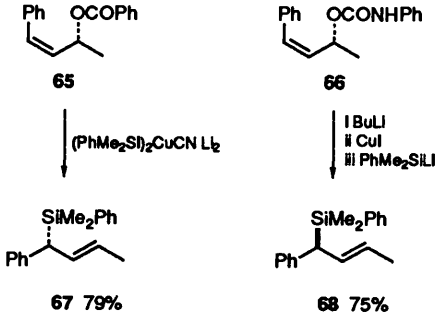
However, the regioisomer of the starting material **58** did give a *different* ratio of the two major products **56** and **57**. In contrast, carbon-cuprates give the *same* ratio of regioisomers from regioisomeric starting materials like **55** and **58**, showing that an intermediate lives long enough to lose the sense of which allylic system it started from.[27] Evidently the silyl-cuprate transfers the silyl group in the reductive elimination step somewhat faster than allylic equilibration. The solution to the regiocontrol problem was to start with a *cis* double bond in the allylic acetate **59**, when the only detectable product was the *trans*-allylsilane **56** with double bond shift. This example is the best of our results, helped as it is by the silyl group entering at the less hindered end of the allylic system. However, the method is regiospecific, with the regioisomeric starting material **60** giving more of the allylsilane **57** with the silyl group adjacent to the larger group, but the degree of regiospecificity is less.

Even better regioselectivity proved to be possible using a different protocol, based on Goering's recipe from carbon-cuprate chemistry.[28] Assembling a hetero-cuprate on a carbamate group ensured high regiospecificity with allylic shift even with a *trans*-double bond, as in the allylic (*E*)-carbamates **61** and **62**, and the regiospecificity was complete with a *cis*-double bond, as in the reactions of the corresponding (*Z*)-carbamates **63** and **64**.

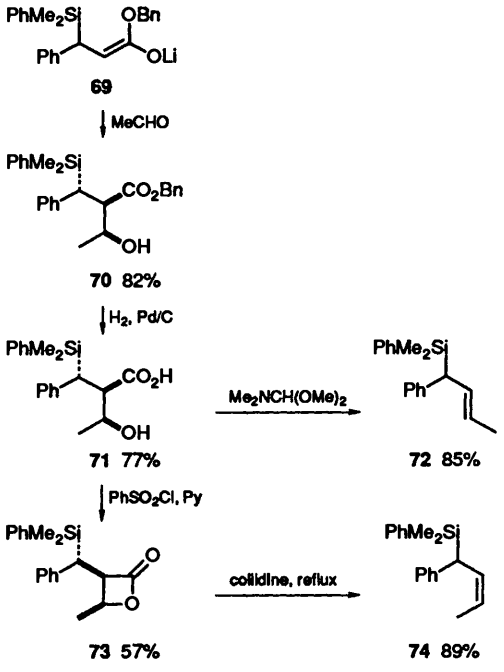
These two methods, the one based on allylic acetates (benzoates are just as good), the other on allylic carbamates, were, as expected by analogy with the corresponding chemistry of carbon-cuprates, stereochemically complementary, the former taking place stereospecifically *anti*, and the latter stereospecifically *syn*. As a result, the appropriate derivatives **65**



and **66** of a single enantiomer of an allylic alcohol can be used to make either enantiomer **67** or **68** of an allylsilane.



The ninth paper[22] describes an alternative synthesis of allylsilanes that are secondary at both ends of the allylic system. This method is completely regioselective, instead of being merely highly regioselective, but the penalty of using it is that it takes several steps, and the overall yield is, in consequence, not high. Nevertheless it has proved immensely useful to us in our work on the S_E2'' reaction of dienylmethylsilanes,[29] and it has allowed us to make, for the first time, an allylsilane with a very high level of enantiomeric purity (>99.9% e.e.).[18] It also has the virtue of giving either the *cis*- or *trans*-allylsilane with nearly equal ease, and is unique in this respect among the many methods of making allylsilanes.[30] The method uses the reaction described in the fourth paper of this series,[10] the aldol reaction between a lithium enolate carrying a silyl group at the β-position such as **69** and an aldehyde. Because the next step is to prepare the carboxylic acid **71** from the ester **70**, we found it necessary to use a benzyl or an allyl ester, because alkaline hydrolysis of a methyl ester induced a substantial amount of retro-aldol reaction. Fortunately, although the allyl and benzyl groups are larger than methyl, they do not seriously compromise the diastereoselectivity of the aldol step, even though that is dependent upon the ester group being small. The 82% yield of the single diastereoisomer of the ester **70** is fairly typical, and actually, in this case, slightly higher than that in the corresponding reaction giving the aldol product **28** from the enolate *Z*-**1** of the methyl ester. We have since found that trimethylsilylethyl is similarly benign in this respect, and, like the allyl and benzyl groups, easily removed without retro-aldol cleavage.[31] The β-hydroxy acid **71** can then be induced to undergo stereospecific decarboxylative dehydration to give, with the appropriate reagents well established in the literature,[32] either the *trans*-allylsilane **72** or, by way of a rather low-yielding step giving the β-lactone **73**, the *cis*-allylsilane **74**.



We briefly tried an alternative sequence using a diphenylphosphine oxide group in place of the carboxylic acid, hoping to use the *syn*-stereospecific Wittig–Horner reaction,[33] and hence avoid the need to break a carbon–carbon bond. Unfortunately, the step corresponding to the aldol reaction was not as highly stereoselective with the phosphine oxide. Furthermore, and worse, the Wittig–Horner step gave none of the allylsilane, taking instead a different but precedented course.

In most of the work described in this series of papers, we used the phenyldimethylsilyl group, both because it is easily introduced using the phenyldimethylsilyl-cuprate reagent and because the phenyl group provides a functional handle making it possible to convert the phenyldimethylsilyl group into a hydroxy group. For some purposes, however, a trimethylsilyl group might be needed. At present, this can only be introduced as a cuprate reagent if one is prepared to make the silyl-lithium reagent in neat HMPA. In order to avoid this problem, we have developed modifications to our allylsilane syntheses, described in the last two papers in the series, for making allylsilanes with a trimethylsilyl group rather than a phenyldimethylsilyl group, without having to use the trimethylsilyl-cuprate reagent. Furthermore, in much of the work described in the earlier papers, we showed that a trimethylsilyl group exerts much the same effect on diastereoselectivity and reactivity as the phenyldimethylsilyl group.

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